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EXAMINER	
EYLER, Y	

ART UNIT	PAPER NUMBER
1642	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary	Application No. 08/813,323	Applicant(s) Baltimore et al
	Examiner Yvonne Eyler	Group Art Unit 1642

☒ Responsive to communication(s) filed on *5/26 and 7/30, 1998*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-20* is/are pending in the application.

Of the above, claim(s) *5-20* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Serial Number: 08/813323

Art Unit: 1642

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-4 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the process of Group II cannot be practiced with another materially different product, as now amended. This is not found persuasive because, as made of record in the Restriction of 2/27/98, the inventions can be shown to be distinct if **either** or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide of Group I may be used in screening assays or to generate antibodies.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5-20 are withdrawn from further consideration, claims 1-4 are under consideration in the application.

Specification

The disclosure is objected to because of the following informalities:

The specification at page 22 contains a sequence disclosure without it's corresponding SEQ ID NO.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in that they only describe the protein of interest by an arbitrary name. While the name itself may have some notion of the activity and function of the protein, there is nothing in the claims which distinctly and definitely describes or points out the protein. Others in the field may isolate the same CRAF1 protein and give such an entirely different name. Applicant should particularly point out and distinctly claim the CRAF1 protein by claiming characteristics associated with the protein. Claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly point out what that protein is.

It is also noted that the instant recitation of an apparently truncated protein by the open language "protein comprising CRAF1 truncated...." is confusing because it isn't clear if more than the truncated protein is contemplated.

The phrase "CD40 mediated cell activation" found in claim 1 is vague and indefinite because the metes and bounds of what is including and definitive of "activation" cannot be determined. Neither the claims nor specification provide a clear definition of what parameters determine or are definitive of cell activation.

Dependent claims 2-4 do not clarify the above indefiniteness.

3. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim one (and therefore dependent claims 2-4) has been amended to recite a truncation of "at least 323 amino acid residues up to 414 amino acid residues" for which the specification fails to provide support. The specification provides support for truncations of about 323 amino acids to about 414 amino acids. Nowhere is it set forth that the truncation must be at least 323 amino acids. The original language indicates that the exact value may vary. Similarly, the specification provides support for truncations of about 414 amino acids, not exactly 414 amino acids, the original specification and claim language indicates that the truncation may be slightly more than 414 amino acids, but must be about 414 amino acids. Thus, the instant amendment alters the claimed invention in scope from that originally disclosed. It is suggested that in order to distinctly claim the truncation as supported by the original disclosure, without introducing indefiniteness, that the claims may be amended to recite amino terminus truncations of 323 amino acids to 414 amino acids residues which is contemplated by the original recitation, or more ideally, to recite the amino acid range of the truncated protein as disclosed on page 5, and in Figure 2.

4. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabling for the invention as broadly claimed. The specification is not enabling for any variant of truncated CRAF1 protein or truncated CRAF1 proteins which inhibit any CD40 mediated cell activation."

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* (230 USPQ 546 (Bd Pat. App. & Int. 1986)).

The instant specification maps the regions responsible for binding to CD40 to the TRAF domain while the function of the other domains present in CRAF1 remains speculative. Further, the specification discloses that truncated CRAF1 proteins retaining the C-terminal TRAF domain (TRAF-C domain) defined by amino acid residues 415-567 of SEQ ID NO: 1 or 2 function as individual CD40 binding units which may have inhibitory properties. The specification further discloses that one specific truncated protein, C26, which consists of amino acid residues 324-567, serves as a dominant negative protein, inhibiting CD40 mediated CD23 upregulation.

Thus, the disclosure of the instant specification supplies sufficient objective evidence and guidance to make it predictable that amino truncated CRAF1 proteins retaining the TRAF-C domain would bind to CD40 with properties similar to the C26 example. However, the specification does provide sufficient guidance and objective evidence that any variant of a CRAF1 truncated protein would reasonably be expected to retain CD40 binding properties and inhibitory

activity. The specification contemplates variants including amino acid substitutions, deletions, or insertions, or other chemical modifications of substituents (pages 8-11). However, the specification fails to provide sufficient guidance (with the exception of conservative substitutions as recited in claim 2) directing one of skill to determine where within the truncated protein the modifications are acceptable and what types of modifications are predicted to result in similar binding and inhibitory activities. The specification discloses only that the TRAF-C domain is necessary, but supplies insufficient information regarding what sequences within this domain may be modified and still predictably result in similar activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of which amino acids can be substituted or modified within a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure and function from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of this protein are lacking, it is unpredictable as to which amino acid substitutions, if any, meet the limitations of the claim. Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers of substituted proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. Therefore, one of ordinary skill would require guidance, such as information regarding the extent of substitution and the location and the specific amino acid changes which would result in the preservation of the stated activity. Therefore, it would require

undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

Additionally, as discussed supra, the phrase "CD40 mediated cell activation" is vague and indefinite because it is not clear what measurable properties of "activation" correlate with CD40 mediated cell "activation," nor is it clear when a cell is determined to be "activated." The specification provides guidance for the determination of inhibition by detecting CD40 mediated CD23 upregulation. There is insufficient guidance or objective evidence to support the correlation of any other measurable "properties" and cell "activation." The specification contemplates that "activation" may include any and all intracellular signaling, immune responses, allergic responses, apoptosis (pages 14-18), yet there is no guidance provided teaching the accurate determination and measurement of "activation" of these processes and their inhibition. Absent further guidance it would require undue experimentation to practice the instant invention and to predictably identify inhibitory truncated proteins as broadly claimed.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Sato et al. (Febs Lett. 358:113-118, Jan. 23, 1995) or Hu et al. (J. Biol.Chem. 269:30069-30072, Dec. 1994-IDS) or Cheng et al. (Science 267:11494-1498, March 10, 1995-IDS).

Sato et al. teach a truncated clone of CAP-1 which encodes little more than the C-terminal region of CAP-1, between amino acid residues 384-540 sufficient to mediate binding to CD40. Sato et al. is silent regarding the inhibitory properties of the truncated protein, however, CAP1 is identical to the instant CRAF1, and the capability of the truncated protein to inhibit CD40 mediated activation events such as CD23 would be an inherent property of the truncated product.

Hu et al. teaches the same CAP1, LAP1, CRAF1 protein, termed CD40bp and a truncated version of only the C-terminal half, from amino acid residue 297-the end, which binds to CD40. Like Sato et al., Hu et al. is silent regarding the inhibitory properties of the truncated protein, however, such properties would be inherent to the product.

Cheng et al. teach that truncated CRAF1, clone C26, identical to the instant product, inhibits CD40-mediated up-regulation of CD23.

It is noted that the proteins designated CRAF1, CAP1 (Sato et al.) CD40bp (Hu et al.), as well as LAP1 (Mosialos et al.-IDS) refer to the same protein, as acknowledged in the instant specification on page 2 and as exemplified by the enclosed sequence data.

Thus, each of Sato et al., Hu et al., and Cheng et al., teach truncated CRAF1 protein products as claimed which would inherently possess the same inhibitory properties.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yvonne Eyler, Ph.D. whose telephone number is (703) 308-6564. The examiner can normally be reached on Monday through Friday from 830am to 630pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703) 308-2731. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**lila.feisee@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Yvonne Eyler

Yvonne Eyler, Ph.D.
Patent examiner
August 12, 1998